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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
SOROUSH, LAYLA	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,507	LIENAU ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-11,19-25,28 and 29* is/are pending in the application.

4a) Of the above claim(s) *11 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-10,19-21,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the Applicant's reply filed August 1, 2007 and March 5, 2007 to the restriction requirement made on January 3, 2007.

Applicant's election of with traverse Group I claims 1-21 and the species Cremophor®EL as the emulsifier, Transcutol®P as the auxiliary emulsifier/solvent, Miglyol® 812 as the lipid, 17beta-HSD as the intestinal enzyme, P-gp- transporter as the intestinal efflux system, and 11 beta-Fluoro-7alpha - {5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluorodecyl)- amino]pentyl} estra- 1,3,5 (10)-trien-3,17 beta-diol as the sterioid.is acknowledged.

Applicant's arguments regarding the restriction requirement have been considered. Applicant's argument that the distinction is not a significant difference is not persuasive. Examiner submit that chapter 800 of the MPEP permits Examiner to make a Restriction Requirement between products, method of treating or using, and process of making. The argument that the groups are classified in the same class and subclass and therefore there is no search burden is not persuasive; because the Restriction Requirement is not solely made on classification but also on an Examination burden. Examiner is aware that if the composition is found allowable, the process claims will be rejoined; please see Restriction Requirement mailed on January 3, 2007 pages 5 and 6.

The requirement is still deemed proper and is therefore made **FINAL.**

Claims 11 are withdrawn from further consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to non-elected subject matter.Claims 22-25 are withdrawn as being dependent on a nonelected group of the restriction requirement.

The addition of claims 28-29 and the cancellation of claims 5-8, 12-18, and 26-27 are herein acknowledged. The claims corresponding to the elected subject matter are 1-4, 9-11, 19-21, and 28-29 are herein acted on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-11 recite the limitation "claim 8." There is insufficient antecedent basis for this limitation in the claim. Claims 10-11 are improperly dependent on claim 8.

Claim 19 recite the limitation "claim 18." There is insufficient antecedent basis for this limitation in the claim. Claim 19 is improperly dependent on claim 18.

Claims 1-4, 9-10, 19-21 and 28-29 contains the trademark/trade name the emulsifier Cremophor®EL, the auxiliary Transcutol®P, the lipid Miglyol® 812. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an emulsifier, auxiliary and lipid, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parikh et al. (WO 99/49848 –IDS) in view of Ferdinando et al.(WO 97/21440 -- IDS).

The claims are examined to the extent that they read on the elected species. Hence, the claims are drawn to a pharmaceutical composition comprising the emulsifier Cremophor®EL, the auxiliary Transcutol®P, the lipid Miglyol® 812, wherein the mass ratio of emulsifier to auxiliary emulsifier and/or solvent (Smix) is 1:1 to 9:1 and the total lipid proportion is > 10-50% (m/m).

Parikh et al. teaches a poorly water soluble anticancer drug paclitaxel in a storage self-emulsifying pre-concentrate in a carrier medium comprising at least one hydrophobic component at least one hydrophilic component, and at least one surfactant (abstract and p. 4 lines 1-6). Examples of surfactants include cremophors particularly Cremophor EL and Cremophor RH40 (p. 4 lines 24-26), propylene glycol mono- and di-fatty acid esters such as Transcutol (p. 5 lines 1-3). Parikh et al. teaches the "appropriate combinations or mixtures of a hydrophobic component, a surfactant and a hydrophilic component with the water insoluble drug are necessary to obtain a stable dispersion with an average particle size of between about 10 nm and about 10 microns

(p. 6 lines 6-10)." The relative proportion of the drug and the other ingredients in the composition of the current invention will vary depending whether it is delivered as a self-emulsifying preconcentrate or after dilution with water depending on the particular ingredients and the desired physical properties of the formulation."

Example 2 is a composition comprising Miglyol 840, Cremophor RH40, and Transcutol. The mass ratio of emulsifier (Cremophor) to auxiliary emulsifier and/or solvent (Transcutol) (Smix) is about 3:1. The amount of Miglyol falls within the range claimed.

The reference fails to exemplify a composition comprising the emulsifier Cremophor®EL, the auxiliary Transcutol®P, and the lipid Miglyol® 812.

Ferdinando teaches a pharmaceutical composition comprising a pharmaceutically acceptable oil, a pharmaceutically-acceptable lipophilic surfactant, a pharmaceutically-acceptable hydrophilic surfactant, and a pharmaceutically-acceptable water-miscible solvent, and a steroid (abstract).

Examples of preferred pharmaceutically acceptable oils include vegetable oils such as soya bean oil, olive oil, and Miglyols 810,812, and 818. Miglyol 812 is preferred (p 5 lines 1-13). Further, examples of pharmaceutically-acceptable lipophilic surfactant Imwitor 988 and 742(p 5 lines 14-23). Pharmaceutically-acceptable hydrophilic surfactants taught by Ferdinando et al. include the condensation products of an alkylene oxide such as ethylene oxide with castor oil or with hydrogenated castor oil for example Cremophors (p 5 lines 25-30 and p 6 lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the

invention to interchange the Cremophor EL and Cremophor RH40; or the Miglyols. The motivation to interchange the Cremophor EL and Cremophor RH40; or the Miglyols 810,812, and 812 is that Cremophor EL and Cremophor RH40; & the Miglyols is because they are similar compositions with similar efficacies and, therefore, the interchangeable use of either one will yield similar results. Additionally, because the reference teaches the genus Transcutol, the species Transcutol®P are rendered obvious by the prior art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the dose range of Parikh et al.'s compound by routine experimentation (see 2144.05 11). The motivation to optimize the dose range of Parikh et al.'s final formulation is because (1) the amounts are deemed to be manipulatable parameters practiced by an artisan to obtain the best possible pharmaceutical results and further Parikh et al.'s teaches that "The relative proportion of the drug and the other ingredients in the composition of the current invention will vary depending whether it is delivered as a self-emulsifying preconcentrate or after dilution with water depending on the particular ingredients and the desired physical properties of the formulation." Therefore, a skilled artisan would have had reasonable expectation of success in achieving the safest clinical outcome by optimizing the dose range of Parikh et al.'s final formulation.

Claims 3 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parikh et al. (WO 99/49848 –IDS) in view of Ferdinando et al.(WO 97/21440 -- IDS) as

applied to claims 1-2, and 9-10 above, and further in view of Sun et al. (Transferrin as a Metal Ion Mediator *Chem. Rev.*, 99 (9), 2817 -2842, 1999).

Parikh et al. and Ferdinand et al. are discussed above.

Parikh et al. and Ferdinand et al. fail to teach a 9:1 ratio as claimed.

A coprecipitate of Cremophor EL, 1,2-propylene glycol in water-free ethanol, and the budotitane in a ratio of 9:1:1 is normally made up prior to administration (p 2837 col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the dose range of Parikh et al.'s compound by routine experimentation (see 2144.05 11). The motivation to optimize the dose range of Parikh et al.'s final formulation is because (1) the amounts are deemed to be manipulatable parameters practiced by an artisan to obtain the best possible pharmaceutical results; Parikh et al.'s teaches that "The relative proportion of the drug and the other ingredients in the composition of the current invention will vary depending whether it is delivered as a self-emulsifying preconcentrate or after dilution with water depending on the particular ingredients and the desired physical properties of the formulation;" and further a Cremophor EL, 1,2-propylene glycol (Transutol is a propylene glycol – p. 5 liens 1-3 of Parikh et al.) in water-free ethanol, and the drug in a ratio of 9:1:1 Therefore, a skilled artisan would have had reasonable expectation of success in achieving the safest clinical outcome by optimizing the dose range of Parikh et al.'s final formulation.

Claims 4, 19-21 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parikh et al. (WO 99/49848 –IDS) in view of Ferdinando et al.(WO

97/21440 -- IDS) as applied to claims 1-2, and 9-10 above, and further in view of Winter et al. (DE 10011883 A1).

Parikh et al. and Ferdinand et al. are discussed above.

Parikh et al. and Ferdinand et al. fail to teach the specific steroid 11 beta-Fluoro-7alpha - {5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluorodecyl)- amino]pentyl} estra- 1,3,5 (10)-trien-3,17 beta-diol, as elected.

Winter et al. is solely used to show that 11 beta-Fluoro-7alpha - {5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluorodecyl)- amino]pentyl} estra- 1,3,5 (10)-trien-3,17 beta-diol is an 1,3,5(10)-triene-3,17.beta.-diol antiestrogen.

It would have been obvious to one of ordinary skill in the art at the time of the invention to interchange the 7-alpha[9-4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17beta-diol for the 11 beta-Fluoro-7alpha - {5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluorodecyl)- amino]pentyl} estra- 1,3,5 (10)-trien-3,17 beta-diol is an 1,3,5(10)-triene-3,17.beta.-diol antiestrogen. The motivation to interchange the 7-alpha[9-4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17beta-diol for the 11 beta-Fluoro-7alpha - {5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluorodecyl)- amino]pentyl} estra- 1,3,5 (10)-trien-3,17 beta-diol is an 1,3,5(10)-triene-3,17.beta.-diol antiestrogen is because they are similar compositions with similar efficacies and, therefore, the interchangeable use of either one will yield similar results.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER